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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,506	09/14/2001	Andreas Huth	SCH-1806	5688

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EXAMINER

LIU, HONG

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/831,506

Applicant(s)

HUTH ET AL.

Examiner

Hong Liu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8,11,12,16 and 17 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8,11,12,16 and 17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claims 1-8, 11-12, 16-17 are pending in this application.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/03 has been entered.

Election/Restriction

Applicants are reminded that they elected the group wherein A, Z, and R1 do not form a single group and A is NR2, and Z is the group shown in claim 1. The recently amended claims 2-6 and 17 still contain unelected subject matter. Applicants are expected to amend the claims to be commensurate to the scope of the elected subject matter.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-8, 11-12, 16-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No.6,448,277. Although the conflicting claims are not identical, they are not patentably distinct from each other because some of the instantly claimed compounds differ from the reference compounds only in the number of -CH₂- links between R₁ and A. It has been long established that a structural relationship varying the size of a linking carbon chain is per se obvious. Specifically, In re Shetty, 195 USPQ 753, In re Wilder, 195 USPQ 426 and Ex parte Gresham 121 USPQ 422 all feature a compound with a C₂-link rejected over a compound with a C₁ link. Similarly, In re Chupp, 2 USPQ 2nd 1437 and In re Coes, 81 USPQ 369 have a C₁ link unpatentable over a C₂ link. Ex parte Nathan, 121 USPQ 349 found the insertion of a C₂H₄ link obvious.

4.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright et al., Chem Abstract 102:78876: The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 93668-03-2.

Claims 1-6, 8, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kovac et al. Chem. Abs. 100: 34516. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 88369-73-7 and 88369-74-8.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 7 is drawn to a method based on KDR and/or FLT antagonism. This claim is interpreted to include any and all disorders associated with this particular mode of action. The claim reads on any and all tumor, psoriasis, eye diseases, diabetic retinopathy, neovascular glaucoma, renal disease, transplant rejection, fibrotic diseases, mesangial-cell-proliferative diseases. However, applicants

disclose on P.1 of specification that VEGF can be the cause of various diseases resulting from persistent angiogenesis, which implies that there could be causes of these diseases other than VEGF. In a recent review article, Carmeliet and Jain discussed the therapeutic perspectives of anti-angiogenic agents in the treatment cancer. The authors pointed out that there are a number of potential problems in the clinical trial of anti-angiogenic agents in the treatment of cancer (Nature, 2000, page 255). The problems include the relevancy of the testing the agent on subcutaneous tumors which are not a common site for human tumors, the distinction of tumor regression and eradication, and the use of agents toxic only to rapidly proliferating cells. There is also uncertainty of long-term side effects of many anti-angiogenic therapies on normal tissues and physiological angiogenesis. The authors concluded that many of these problems can only be addressed with further carefully planned studies. The above discussion makes it clear that, at least as of 2000, much more than routine experimentation would be required to find a compound that will be really effective in treating cancer associated with angiogenesis. As of 2000, there was only the potential, and that success would require future development, i.e. more than routine experimentation.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation and use of compounds wherein Z and R1, Ra and Rb, Rc, and Rd do not form a bridge, does not reasonably provide enablement for preparation and use of compounds wherein Z and R1, Ra and Rb, Rc, and Rd form a bridge. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein Z and R1, Ra and Rb, Rc, and Rd form a bridge with 3 ring members or up to 3-C members. While many compounds are disclosed, there is insufficient guidance for preparing additional VEGF antagonist which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein Z and R1, Ra and Rb, Rc, and Rd do not form a bridge have been made.

Furthermore, testing data is limited to a number of compounds not considered to be representative of all the possible compounds encompassed by the claims. Examples should be of sufficient scope as to justify the scope of the claim. However, the generic claims are much broader in scope than is represented by the testing. The definitions of the various R, Z variables embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples" fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See *In re Fouch*, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view

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of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability” have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1). There is a double bond before NR10, NR2, NR9 or N (pages 9 and 10).

However, there should be a single bond connecting to these groups. Clarification is required.


2). In claim 1 in the definition of Ra-Rf, the phrase “and/or” makes it difficult to determine which R group is connected to which R group to form a bond or bridge.

3). The phrase "with Ra-Rf from Z, or to R1, forms a bridge...(page 12, line 3)" is not understood.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (571) 272-0669. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM.

If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisors, Mukund Shah can be reached at (571) 272-0674. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 358-1235.


Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

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March 18, 2004